REMARKS

Claims 2-3, 5-9 and 17 are pending in the subject application with claims 11-16 and 18-23 withdrawn from consideration. Applicants have not cancelled, added or amended any claims herein

Claims Rejected Under 35 U.S.C. §103(a)

Claims 2,3 and 5-9

The Examiner rejected claims 2, 3, and 5-9 under 35 U.S.C. §103(a) as allegedly obvious over Ronai et al. (*Biochem. Biophys. Res. Comm.*, 1979, 91:1239-1249) in view of Abbruscato et al. (*J. Neurochem.*, 1997, 69:1236-1245) and Kanai et al. (*J. Biol. Chem.*, 1998, 273:23629-23632). The Examiner asserted that it would have been obvious to one of skill in the art, in light of Kanai et al., to substitute methionine for the alanine in biphalin taught by Abbruscato et al. in order to mimic the tetrapeptide taught by Ronai et al. The Examiner also noted, in an Interview Summary issued October 15, 2008 in connection with the above-identified application regarding an October 6, 2008 interview in reference to, inter alia, applicants' argument of the unexpected duration of anti-nociception of the claimed dimer versus biphalin, that applicants intended to file a declaration showing the unexpected results.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that the claimed dimer shows an unexpectedly long duration of anti-nociception over biphalin

disclosed in the cited art. In support of this assertion, applicants attach hereto as **Exhibit 1** a DECLARATION UNDER 37 C.F.R. §1.132 OF ANDRZEJ W. LIPKOWSKI. Professor Lipkowski is named as inventor on the subject application. The attached Declaration presents results which show that the duration of anti-nociception achieved by the claimed dimer could not have been predicted by one of ordinary skill in the art based on the duration of anti-nociception elicited by biphalin versus the "biphalin monomer".

As disclosed in the Declaration, the "biphalin monomer" and the monomer of the claimed dimer achieved comparable duration of anti-nociception. However, biphalin and the claimed dimer did not exhibit comparable duration of anti-nociception. In fact, the claimed dimer showed an improvement in duration of anti-nociception over the biphalin.

Specifically, while the monomers Tyr-D-Ala-Gly-Phe-NH_2 and Tyr-D-Met-Gly-Phe-NH_2 show comparable duration of anti-nociception, (see Exhibit 1, para. 3), biphalin shows 30% anti-nociceptive activity as measured in the rat tail-flick test at 30 minutes after administration and zero anti-nociceptive activity at 120 minutes after administration (see Exhibit 1, para. 4). Because the duration of the anti-nociception of the monomers is comparable, one would expect the claimed dimer to show a pattern of anti-nociception similar to that of biphalin. However, at the same dosage as biphalin, the claimed dimer (Tyr-D-Met-Gly-Phe-NH-)$_2$ actually shows 55% anti-nociceptive activity at 30 minutes after administration, and is still eliciting 30% anti-

nociceptive activity at 120 minutes after administration (see Exhibit 1, para. 5). This sustained anti-nociception property is unpredictable based on the prior art. Moreover, it is an improvement over the prior art compounds.

Applicants thus maintain that the compound as claimed is not obvious over the combination of cited art. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims 2,3, 5-9 and 17

The Examiner rejected claims 2, 3, 5-9 and 17 under 35 U.S.C. §103(a) as allegedly obvious over Ronai et al. (*Biochem. Biophys. Res. Comm.*, 1979, 91:1239-1249) in view of Abbruscato et al. (*J. Neurochem.*, 1997, 69:1236-1245) and Kanai et al. (*J. Biol. Chem.*, 1998, 273:23629-23632) in further view of Hill et al. (U.S. Patent No. 5,880,132), Bock et al. (EP 0434369) and Ornstein (U.S. Patent No. 5,356,902). The Examiner asserted that Ornstein, Hill and Bock et al. teach stimulatory amino acids, tachykinins and cholecystokinin receptor antagonists, and that Abbruscato et al. teaches biphalin, and that it would have been obvious to one of skill in the art to combine the teachings of the cited art to arrive at the invention as claimed. The Examiner also noted, in an Interview Summary issued October 15, 2008 in connection with the above-identified application regarding an October 6, 2008 interview in reference to, inter alia, applicants' argument of the unexpected duration of anti-nociception of the claimed dimer versus biphalin, that applicants intended to file a declaration showing the unexpected results.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that the claimed dimer shows an unexpectedly long duration of anti-nociception over biphalin disclosed in the cited art. In support of this assertion, applicants attach hereto as **Exhibit 1** a DECLARATION UNDER 37 C.F.R. §1.132 OF ANDRZEJ W. LIPKOWSKI. Professor Lipkowski is named as inventor on the subject application. The attached Declaration presents results which show that the duration of anti-nociception achieved by the claimed dimer could not have been predicted by one of ordinary skill in the art based on the duration of anti-nociception elicited by biphalin versus the "biphalin monomer".

As disclosed in the Declaration, the "biphalin monomer" and the monomer of the claimed dimer achieved comparable duration of anti-nociception. However, biphalin and the claimed dimer did not exhibit comparable duration of anti-nociception. In fact, the claimed dimer showed an improvement in duration of anti-nociception over the biphalin.

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Applicants thus maintain that the compound as claimed is not obvious over the combination of cited art. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

If a telephone interview would be of assistance in advancing prosecution of the subject application, the undersigned attorney invites the Examiner to telephone them at the telephone number provided below.

No fee, apart from the enclosed $555.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Communication. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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EXHIBIT 1

EXHIBIT A